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(54) Title: TRANCE REGULATION OF CHONDROCYTE DIFFERENTIATION

(57) Abstract: Disclosed are therapeutic methods of treating a mammal, e.g., a human patient, having a disease, disorder or condition characterized by abnormal (excessive or insufficient) cartilage growth or skeletal growth. The methods include inhibiting or supplementing activity of TRANCE or TRAF6 in chondrocytes in vivo or ex vivo. Also disclosed are methods of diagnosing a cartilage disorder. The method includes detecting an elevated or reduced level of TRANCE, RANK, or TRAF6 in chondrocytes. Also disclosed are methods of identifying a compound that increases or decreases proliferation of chondrocytes, or a compound that promotes differentiation, e.g., maturation, of chondrocytes.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/26101

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C07H 21/04, 21/02; A61K 48/00; C12P 19/34

US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.1, 325, 375; 536/23.1, 24.5, 24.3, 24.31, 24.33; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN, MEDLINE, CAPLUS, LIFESCI, EMBASSE, USPATFULL, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KINPARA ET AL. Osteoclast Differentiation Factor in Human Osteosarcome Cell Line. Journal of Immunoassay. January 2000, Vol. 21, No. 4, pages 327-340.	1-33
Y, P	PEARSE ET AL. Administration of the Trance-Antagonist TR-FC Limits Myeloma-Induced Bone Destruction. Blood. 16 November 2000, Vol. 96, No. 11, Part 1, page 549a.	1-33
Y	NAKAGAWA ET AL. RANK Is the Essential Signaling Receptor for Osteoclast Differentiation Factor in Osteoclastogenesis. Biochemical and Biophysical Research Communications. 16 March 1998, Vol. 253, pages 395-400.	1-33

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

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Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3250	Authorized officer <i>Felicia D. Roberts for</i> KAREN A. LACOURCIERE Telephone No. (703) 308-1235

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NAGAI ET AL. Cancer Cells Responsible for Humoral Hypercalcemia Express mRNA Encoding a Secreted Form of ODF/TRANCE That Induces Osteoclast Formation. Biochemical and Biophysical Research Communications. 16 March 2000, Vol. 269, pages 532-536.	1-33
Y	KOBAYASHI ET AL. Tumor Necrosis Factor A Stimulates Osteoclast Differentiation by a mechanism Independent of the ODF/RANKL-RANK Interaction. J. Exp. Med. 17 January 2000, Vol. 191, No. 2, pages 275-285.	1-33
Y	TAKAI ET AL. Transforming Growth Factor-B Stimulates the Production of Osteoprotegerin/Osteoclastogenesis Inhibitory Factor by Bone Marrow Stromal Cells. The Journal of Biological Chemistry. 16 October 1998, Vol. 273, No. 42, pages 27091-27096.	1-33
Y	WO 99/29865 A2 (THE ROCKEFELLER UNIVERSITY) 17 June 1999 (17.06.99), see entire document.	1-33
Y	WO 97/40192 A1 (TULARIK, INC.) 30 October 1997 (30.10.97), see entire document.	1-33
Y	WO 98/46751 A1 (AMGEN INC.) 22 October 1998 (22.10.98), see entire document.	1-33

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